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EXAMINER

SAUNDERS, DAVID A

ART UNIT

PAPER NUMBER

1644

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 074,695	Applicant(s) OLSSON et al
Examiner SAUNDERS	Group Art Unit 1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 10/28/04
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 20-21, 30-31 is/are pending in the application.
- Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 20-21, 30-31 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____
 - ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

Office Action Summary

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The claims pending are 1, 7, 13-21 and 30-31.

Applicant's election without traverse of Group IV (claims 20-21 and 30-31) in the reply filed on 10/28/04 is acknowledged.

It is noted that Lennart Olsson signed the response of 10/28/04. This response is taken to be from the assignee. See lower left of page, below the signature. It is noted that Lennart Olsson has been authorized to sign on behalf of the assignee, in Power of Attorney papers submitted on 6/19/02.

The specification is objected to because of the following informalities: At page 1, the continuation data was amended by a preliminary amendment filed 2/11/02. This data is incomplete, because Pat. Nos. corresponding to the Ser. Nos. are not provided.

In Table 2, the headings of the two most right columns are confusing. Are "PEPIr" and "peplr" the same or different peptides? Examiner finds no reference to "PEPIr" elsewhere in the text.

Appropriate correction is required.

Claims 20 and 30-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 20 the limitations of claim 13 must be incorporated into step a).

If claim 13, as presently recited, were to be incorporated into claim 20 then claim 20 would become indefinite, because it is unclear what the modification recited in claim 13 may be. Line 2 thereof recites that the "modification comprises an amino acid sequence substitution, insertion or deletion"; this implies that the modification can be in

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merely one amino acid of the sequence. Line 4 thereof recites that the "modified sequence is of at least about 8 amino acids and less than 40 amino acids; this implies that the modification must be in at least 8 amino acids. So, is the modification in one or in 8 amino acids? The recitation of claim 13 would be clearer if, at line 4, "modified sequence" were to be recited as - - internalization sequence - -.

In claim 30, steps a) and b) "bioactive peptide" is unclear, because the activity of this peptide is not defined.

In claim 30, the limitations of claim 1 must be incorporated into steps a) and b).

Claim 31 depends from cancelled claim 22. Even if claim 22 were pending, claim 31 would be unclear, because there is no antecedent basis for "said sequence of an alpha-1-domain..." in any claim from which 22 has depended.

As a result of problems associated with the dependency of claim 31, it is deemed impossible to further examine this for enablement/description, over prior art, or for double patenting.

Claims 20-21 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not adequately described what an "internalization sequence" is in structural terms such that one would know a given sequence of amino acids constitutes an "internalization sequence".

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Applicant's disclosure has defined the internalization sequence in terms of its function (page 5, lines 8⁺). This is an inadequate description. Univ. of California V. Eli Lilly 43 USPQ2d 1398. The only description, in terms of structure, is that an internalization sequence has homology to the sequence of an alpha – 1 domain of MHC classes I (page 6, lines 11+). While this appears to provide a description of structure, this is inadequate for the following reasons.

1) The alpha-1 domain of MHC class I is highly variable. Applicant's disclosure notes that the sequences within the alpha-1 domain that are of interest be within "the polymorphic regions" (page 6, line 16). Applicant's disclosure then exemplifies one such sequence (SEQ ID No: 1) at page 6, line 19) and then bases all of the ensuing examples on peptides having homology to this sequence. However, this one alpha-1 domain sequence is not representative of the genus of all alpha-1 domain sequences because there is a high degree of variability therein. -- e.g. between HLA-A, B and C, as well as between polymorphisms within each of HLA-A, B and C.

2) The term "homology" is all encompassing. Applicant's examples (Table 1) show peptides that are "homologous" based upon a "similarity" percentage. Applicant's disclosure contemplates that the sequence similarity should be "at least 35%" (page 7, line 7,). What is calculated as a percent similarity however depends upon the arbitrarily chosen settings of various parameters used in the calculation. Adjustment of these parameters can render a given oligopeptide as being above or below the 35% cut-off point.

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3) Applicant contemplates modifications of the sequences selected by homology. Applicant contemplates amino acid substitutions within the internalization sequence (page 8, lines 7⁺); applicant appears to set some limits therein, but there is no limit upon the number of conservative substitutions at "non-critical residues" (page 8, line 16). It is to be further noted that the "non-critical residues" are defined by function (e.g. page 8, lines 2-6 and 9-10). Applicant also contemplates non-conservative substitutions (page 8, lines 20-21). In addition applicant contemplates modifications in terms of insertions and deletions (page 8, lines 4-5). Applicant has merely limited what is permitted for these modifications by way of a functional definition (page 8, lines 2-3).

In summary, applicant is describing "internalization sequences" based upon homology to an MHC class I alpha-1 domain, which itself is highly polymorphic. From this polymorphic basis, one then identifies "internalization sequences" based upon "homology" calculations, which can give results that vary depending upon what parameters are used in the calculation. Once thus identified these internalization sequences can be further "modified". At this point one would have little idea as to whether a given oligopeptide sequence should or should not be considered as an "internalization sequence".

Applicant's definition of an "internalization sequence" is thus based merely upon homology to what is itself a highly polymorphic sequence and upon the function of what sequences have "homology". Applicant has not pointed out any sequence motif or tertiary structural features that would permit one to identify a given sequence as a member of the genus of "internalization sequences". From the ten exemplified such

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sequences (page 7, lines 9-19 and Table 1), no sequence motif can be discerned that would define these sequences structurally. The ten exemplified "internalization sequences" are thus not representative of the genus.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 21 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Olsson et al (WO 95/05189).

Olsson et al teach drug-screening assays at pages 18-27. Therein they do not refer to an "internalization sequence"; however, what they do inherently anticipates.

First, it is noted that Olsson et al teach screening for drugs that modulate reception internalization; see page 18, line 31 – page 19, line 18, for example.

Second, Olsson et al use the same reagents as those used instantly. Note the competitive binding assay taught at page 19, line 19 – page 21, line 12. The "Peptide derived from class I MHC antigen and having modulatory activity" (page 19, lines 19-21) corresponds to the "bioactive peptide" used in steps a) and b) of instant claim 30.

Olsson et al describe such peptides as including those derived from the alpha-1 region of MHC class I, most particularly in the region spanning residues 60-85, etc.; see page

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7, lines 9-11. This corresponded precisely to what applicant discloses instantly as being the sequence within MHC class I that corresponds to an internalization sequence (page 6, lines 11+). This peptide of Olsson et al is bound to a support.

The "oligopeptide used by Olsson et al (page 20, lines 10-13) corresponds to the instant "receptor-derived oligopeptide" used in steps a) and b) of instant claim 30. It has "substantially the same amino acid sequence as the oligopeptide bound to the support" (i.e. that peptide noted in the above para.). From the disclosure of such oligopeptides at page 7 of Olsson et al, it is clear that oligopeptides of "at least about 8 amino acids and less than 40 amino acids" (as recited in instant base claim 1) were contemplated as constituting the most preferred embodiment. This oligopeptide is labeled.

It is further noted that, since the oligopeptide on the solid phase (support) and the oligopeptide that is labeled are of "substantially the same amino acid sequence (page 20, lines 12-13), the examiner could equally well state this rejection with the interpretation that the solid phase oligopeptide of Olsson et al corresponds to the instant "receptor derived oligopeptide" and that the labeled oligopeptide of Olsson et al corresponds to the instant "bioactive peptide".

The oligopeptide on the solid phase, the oligopeptide in solution (i.e. the one that is labeled) and the drug candidate are combined, and the degree of binding of the drug candidate to the solid phase is determined by competition. See page 20, lines 9-12 and page 21-lines 1-12. This corresponds to step a) of instant claim 30.

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Third, Olsson et al also conduct a binding test with the active peptide (The one on the solid phase) and the labeled peptide (the one in solution) are added together without a drug candidate (page 21, lines 5-6). This corresponds to step b) of instant claim 30.

Fourth, Olsson et al compare the binding of the test sample including the drug candidate and the test sample without a drug candidate (page 21, lines 1-9).

Fifth Olsson et al draw the conclusion that drug candidates observed to be capable of competitive binding "may mediate modulation of cell surface expression of a receptor with a peptide – like activity." See page 21, lines 10-21. It is to be noted that the term "modulation of all surface expression" encompasses modulation of internalization. See page 6, lines 1-21.

Regarding instant claim 21, applicant is again referred to the above noted competitive binding assay at page 19, line 19- page 21, line 12. Olsson et al teach that the solid phase reagent may be "a substantially purified class –I MHC antigen (page 21, lines 21-22); this would correspond to the "cell surface receptor" used in instant claim 21. The labeled oligopeptide of Olsson et al (page 20, lines 9+) would have the inherent property of binding to a sequence within the solid phase MHC which, serves as an "internalization sequence". This follows from the fact that the oligopeptide that is labeled would associate with its corresponding sequence within the MHC. See Olsson et al at page 19, lines 2-10. It is this sequence that applicant has instantly characterized as an "internalization sequence".

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When candidate drug and labeled oligopeptide are added to the solid phase MHC class I antigen (page 20, lines 9-12), one would be conducting the method of instant claim 21. It is to be noted that the competitive binding assay of cancelled dependent claim 22 would precisely involve doing what Olsson et al teach.

The rejection is made on the basis of inherency. While Olsson et al do not teach an "internalization sequence" *ipsis verbis*, the oligopeptides that they use inherently have sequences corresponding to the instant "internalization sequence". The competitive binding assays of Olsson et al would thus identify the same candidate drugs as those identified instantly. By now reciting "internalization sequence" applicant is merely referring to an inherent property of a previously used composition. This does not provide a basis for patentability. *In re Spada* 15 USPQ2d 1655. *In see Schoenwald* 22 USPQ2d 1671.

With respect to instant claim 31, the examiner does not know how to reject it, because of its improper dependency. If it were recited as dependent from either or with of claims 21 and 30, it is deemed it would be anticipated (shown somewhere in the large disclosure of Olsson et al) or at the least obvious, since it is derived from the region of MHC class I antigens/ receptors noted by Olsson et al as of interest (page 7).

Also the examiner has no idea as to what particular H-2 or HLA antigen instant SEQ ID NO: 1 of claim 31 might have been derived from. Page 6, lines 18-21 of the instant specification appears to state that this is SEQ ID NO: 1 of Pat. 5,385,888; however, the examiner does not find SEQ ID NO: 1 of the instant disclosure and SEQ

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ID NO: 1 of the "888 Pat. to be the same. Clarification is requested, in the event that claim 31 is further prosecuted.

Instant claim 20 is allowable over Olsson et al. This reference teaches nothing about providing the cell used in step a). That is, there is no teaching that one should modify any sequence corresponding to the instant "internalization sequence", as would be required by base claim 13. Note that Olsson et al teach competitive binding assays using whole cells (page 22, lines 28+); that express MHC class I; however, they teach nothing about using cells with modified MHC I. Also Olsson et al teach an assay employing cells, with the addition of a ligand of a receptor (page 23, lines 34+); this assay does not use cells with a modified receptor.

Claims 21 and 30 are rejected under 35 U.S.C. 102(f) and (g) as being anticipated by Olsson et al (5,639,548 or 5,865,888):

The two Olsson et al US Patents have disclosures corresponding to that of Olsson et al (WO 95/05185) cited supra. Since the inventive entity instantly differs from the two Olsson et al US Patents, rejections under 102 (f) and (g) are properly stated.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-21 and 30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 9 of U.S. Patent No. 6,346,390. Although the conflicting claims are not identical, they are not patentably distinct from each other because Instant claim 20, if read with claim 13 incorporated into step a), follows the essential format of issued claim 1.

The only difference is that, instantly, the modification of the cell surface receptor of the cell used in step a) is limited to a modification to a sequence "of at least about 8 amino acids and less than about 4, amino acids," while, for the issued claims, the modification of the cell surface receptor is not thus limited. The use of a cell with a receptor modified according to the instant limitations of claim 20 is however, certainly encompassed by what is generically recited with respect to a modified receptor in issued claim 1. Thus a disclaimer is required to assure that any patent issued instantly would remain commonly owned with the patent that has been issued.

Instant claim 21 essentially follows the format of issued claim 9. The key difference is that instant claim 21 generically recites "combining a cell surface receptor", while issued claim 9 recites "combining at least a portion of said cell surface receptor. The open language of the issued claim permits the use of the whole cell surface receptor, as well as simply a "portion" thereof. Thus at least instant claim 21 would encompass some embodiments of issued claim 9. A disclaimer is required to assure that any patent issued would remain commonly owned.

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Like considerations apply to instant claim 21, when compared to issued claim 15. Additionally instant claim 21 must be considered to encompass the other limitation of issued claim 15 that is not in instant claim 21 – namely the limitation that an oligopeptide is added along with the candidate agent. This limitation of issued claim 15 can be considered as referring to the addition of an oligopeptide, which would compete with the added agent for binding to the internalization sequence of the cell surface receptor. Since a competitive binding assay is a well-known way of “determining the binding of a candidate agent to the internalization sequence of the cell surface receptor” (instant claim 21), what is reacted in issued claim 15 is encompassed by instant claim 21.

Regarding instant claim 30, this is to be compared against issued claim 15. In instant claim 30, step b), when read with the limitations of instant claim 1 incorporated therein, essentially corresponds to the “combining” step of issued claim 15. Instant claim 30 has the additional feature of providing for a additional binding step (i.e. step a)) in which association of the “bioactive peptide” (corresponding to “a portion of said cell surface receptor” in issued claim 15) and the “receptor derived oligopeptide” (corresponding to the “oligopeptide” of issued claim 15) is determined without the presence of a candidate agent. This determination is then compared relative to that for binding determined for step b). This is essentially a comparison of an experimental result (with agent) against a control (with agent); such is art conventional in screening. A disclaimer is thus required.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Saunders whose telephone number is (571) 272-0849. The examiner can normally be reached on Monday to Thursday from 8 AM to 5:30 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/LR
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PRIMARY EXAMINER
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